

Remarks

Applicant has cancelled, without prejudice, all claims directed to cyclopropyl analogs of epothilone, viz., Claims 1-3, 9, 11-13 and 27. The claims directed to cyclopropyl analogs of epothilone will be pursued in a continuing application. Claims are directed to epoxide analogs of epothilone, viz., Claims 15-18 and 29, are pending and have been allowed. A Notice of Allowance is requested with respect to the pending claims, viz., Claims 15-18 and 29.

Rejection under 35 USC §103(a):

Claims 1-3, 9, 11-13 and 27 were finally rejected under 35 USC §103(a) as obvious over Vite (WO99/54318), Nicolaou (WO99/67252), and/or Klimko (WO2003/026744). Applicant traverses this basis of rejection.

Vite (WO99/54318) discloses a synthetic procedure whereby epothilones A and B are deoxygenated at the epoxide ring (WCl_6 , $n\text{-BuLi}$) and then cyclopropanated under mild conditions. This deoxygenation process occurs with retention of the epoxide geometry. If the epoxide was *cis*, then the double bond will be *cis* and if the epoxide was *trans*, then the newly formed double bond will be *trans*. This methodology is very limited in scope as the starting materials are the natural products or epothilones containing an epoxide or having only a 12,13- unsaturation. One could not make the instantly claimed compounds using this methodology. The suggestion of Vite (WO99/54318) is limited by the limitations of its disclosed methodology. More particularly, Vite (WO99/54318) discloses how to derivatize the naturally occurring R_8 group but does not disclose how to introduce new groups into this position. Because of these limitations, Vite (WO99/54318) neither discloses nor suggests any of the compounds of claims 1-3, 9, 11-13 and 27 of the present application. Accordingly, claims 1-3, 9, 11-13 and 27 of the present application are patentably unobvious over

Vite (WO99/54318) and are patentably unobvious over Vite (WO99/54318) in combination with either Nicolaou (WO99/67252), and/or Klimko (WO2003/026744).

Although Nicolaou (WO99/67252) discloses the compound of Claim 14 (now cancelled), Nicolaou (WO99/67252) does not disclose or suggest the advantageous activity of this particular compound and does not disclose or suggest structural elements of sulfur containing tails employable for making analogs for the compound of Claim 14. Accordingly, there is no suggestion to make analogs of the compound of Claim 14. Claims 1-3, 9, 11-13 and 27 of the present application are patentably unobvious over Nicolaou (WO99/67252) because of this lack of suggestion.

Klimko (WO2003/026744) discloses a method for treating ophthalmic conditions using prior art epothilones, including, *inter alia*, the epothilones of Vita. No new epothilones are disclosed by Klimko. Applicant's comments regarding Vite (WO99/54318), Nicolaou (WO99/67252) are also applicable to Klimko (WO2003/026744). Claims 1-3, 9, 11-13 and 27 of the present application are patentably unobvious over Klimko (WO2003/026744).

However, Applicant's cancellation of claims 1-3, 9, 11-13 and 27 obviate this basis for rejection.

Summary:

All rejected claims, viz., claims 1-3, 9, 11-13 and 27, have been cancelled. Only allowed claims remain pending in this case, viz., claims 15-18 and 29. A Notice of Allowance with respect to Claims 15-18 and 29 is requested.

Respectfully submitted,

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Date


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